Ceylon College of Physicians

CLINICAL PRACTICE GUIDELINES

Sri Lanka College of Endocrinologists

DIABETES MELLITUS MANAGEMENT GUIDELINES

January 2018
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Abbreviations

ABI: Ankle Brachial Index
ACEI: Angiotensin Converting Enzyme Inhibitor
AIDS: Acquired Immunodeficiency Syndrome
ARB: Angiotensin Receptor Blocker
BIDS: Basal insulin day time Sulfonylurea regimen
BMI: Body Mass Index
CAD: Coronary Artery Disease
CIDP: Chronic Inflammatory Demyelinating Polyneuropathy
CKD: Chronic Kidney Disease
CLI: Critical Limb Ischemia
CV risk: Cardio Vascular risk
CVD: Cardio Vascular Disease
DCCT: Diabetes Control and Complications Trial
DKA: Diabetic Ketoacidosis
DM: Diabetes Mellitus
DPN: Diabetic Peripheral Neuropathy
DPP-4 Inhibitor: Dipeptidyl Peptidase-4 Inhibitors
DVT: Deep Vein Thrombosis
eGFR: Estimated Glomerular Filtration Rate
ESR: Erythrocyte Sedimentation Rate
ESRD: End Stage Renal Disease
FDA: Food and Drug Administration
FPG: Fasting plasma glucose
GDM: Gestational Diabetes Mellitus
GI: Gastrointestinal
GLP-1RA: Glucagon-like peptide-1 Receptor Agonist
HbA1C: Glycosylated Haemoglobin
HDL: High Density Lipoprotein
HIV: Human Immune Deficiency Virus
HONK: Hyperosmolar Non Ketotic Coma
ICU: Intensive Care Unit
IM: Intramuscular
IV: Intravenous
IADPSG: International Association of Diabetes and Pregnancy Study Groups
LDL: Low density lipoprotein
MODY: Maturity-onset diabetes of the young
NG: Nasogastric
NGSP: National Glycohemoglobin Standardization Program
NPDR: Non Proliferative Diabetic Retinopathy
NPH: Neutral Protamine Hagedorn (Isophane insulin)
OGTT: Oral Glucose Tolerance Test
PN: Peripheral Neuropathy
PG: Plasma Glucose
PPG: Postprandial Glucose
RBG: Random Blood Glucose
RDA: Recommended Daily Allowance
SBP: Systolic Blood Pressure
SGLT2 inhibitor: Sodium Glucose co Transporter 2 inhibitor
SMBG: Self Monitoring Of Blood Glucose
SNRI: Serotonin-Norepinephrine Reuptake inhibitors
T1DM: Type 1 Diabetes Mellitus
T2DM: Type 2 Diabetes Mellitus
TCA: Tricyclic Antidepressant
TG: Triglyceride
TZD: Thiazolidinediones
U: units
UACR: Urine Albumin Creatinine Ratio
VEGF: Vascular Endothelial Growth Factor
WHO: World Health Organization
# TABLE OF CONTENTS

1. Introduction

2. Classification

3. Diagnosis

4. Screening for Diabetes

5. Clinical Evaluation

6. Management of Type 2 Diabetes

7. Management of Cardiovascular risk factors

8. Management of complications of diabetes

9. Management of Diabetic Emergencies

10. Management of Diabetes in special situations
1. INTRODUCTION

This guideline is developed as a part of clinical practice guidelines produced by the Ceylon College of Physicians in collaboration with Sri Lanka College of Endocrinologists. The aim of this guideline is to guide all the doctors involved in the management of Diabetes in Sri Lanka. This is prepared according to the existing guidelines published by various international professional organizations including American Diabetes Association (ADA) and modified according to the local data to make it suitable to use in local context.

Diabetes mellitus is a metabolic disorder of multiple aetiology. The disease is characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both. Continuing global pandemic of diabetes exacts huge costs both in terms of human suffering and economics. By 2040, the worldwide prevalence is projected to be 642 million, a 55% increase compared to 2015(1). Sri Lanka has not been spared from this pandemic and a similar upward trend in prevalence has been observed in local studies. Of note is a dramatic rise in urban prevalence. Overall prevalence of diabetes for Sri Lankans aged >20 years was 10.3% according to Sri Lanka diabetes and cardiovascular study (SLDCS) conducted 10 years back in 2006 with projected prevalence of 13.9% for year 2030 (2). Diabetes prevalence was reportedly higher among urban Sri Lankan population (16.8% in SLDCS and 20.3% for males and 19.3% for females in Ragama study) (2,3). Recent Colombo urban study reported a rise of urban prevalence of diabetes from 16.8% to 27.1% and a rise of prediabetes from 13.6% to 30.1% over last 10 years (2,4). Therefore an alarming increase in complications of diabetes, both microvascular disease and macrovascular disease will be seen unless urgent measures are taken to prevent them.

Diabetes Mellitus is a major risk factor for chronic kidney disease, young onset blindness and cardiovascular diseases. Considerable percentage of type 2 DM patients are unaware of the diagnosis and may have complications of diabetes at the time of diagnosis. Screening and early detection of diabetes, proper lifestyle modifications, optimizing management according to individualized targets, overall cardiovascular risk reduction, and timely referrals will help to prevent morbidity and mortality related to diabetes which is also a major burden to our country’s economy.
2. CLASSIFICATION

Diabetes can be classified into four main subtypes (5).

1. Type 1 diabetes (Type 1 DM)

Type 1 DM (T1DM) is due to absolute deficiency of insulin due to pancreatic β-cell destruction. In majority this occurs as a result of cell mediated auto-immune destruction of pancreatic β-cells. Islet cell auto antibodies, glutamic acid decarboxylase (GAD65) antibodies and auto-antibodies to insulin are some of the bio-markers present in these patients. In a small number of patients the aetiology is unknown.

2. Type 2 diabetes (Type 2 DM)

Type 2 DM (T2DM) accounts for 90-95% of all diabetic patients and is due to relative insulin deficiency along with insulin resistance. Although the exact aetiology is not clear, the risk of developing T2DM is associated with obesity and physical inactivity (Table 3). It has a strong genetic predisposition than T1DM.

3. Gestational diabetes mellitus (GDM)

GDM is diabetes diagnosed in the second or third trimester of pregnancy that is not clearly type 1 or type 2 diabetes. Women with diabetes in the first trimester of pregnancy are classified as pre-existing diabetes.

4. Specific types of diabetes

There are several specific types of diabetes such as monogenic diabetes syndromes, diseases of the pancreas and drug-induced diabetes.

- Monogenic diabetes syndromes are due defects of β cell function and include Neonatal diabetes and maturity-onset diabetes of the young (MODY)
- Diseases that involve the exocrine function of pancreas e.g. cystic fibrosis, chronic pancreatitis
- Drug-induced diabetes is due to use of diabetogenic drugs such as steroids and treatment of HIV/AIDS

Classification of diabetes is helpful in deciding on the therapy. However, there may be difficulties in determining the type of DM at the time of diagnosis e.g. type 1 DM may occur in adults and type 2 DM may be seen in children.
3. DIAGNOSIS

3.1 Diagnostic tests
Following tests can be used for diagnosis of Diabetes mellitus.

- **Fasting plasma glucose (FPG)** – Fasting is defined as no caloric intake for at least 8 hours and for maximum of 12 hours.

- **Two hour plasma glucose (2-hr PG) in 75 gm oral glucose tolerance test (OGTT)** - This test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.

- **HbA1c** - Although this is convenient as it does not require fasting, it is costly and has limited availability in resource poor settings. HbA1C must be measured using a validated assay standardized to the National Glycohemoglobin Standardization Program-Diabetes Control and Complications Trial reference. Further, HbA1C levels can vary with age, ethnicity, anaemia, haemoglobinopathies, haemolysis, blood loss and in severe hepatic and renal disease.

- **Random blood sugar (RBS)** – RBS can be used for diagnosis of diabetes in the presence of symptomatic hyperglycaemia.

3.2 Criteria for diagnosis (Table 1) (5)

<table>
<thead>
<tr>
<th>Table 1:Criteria for the diagnosis of diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>FPG &gt;126 mg/dL (7.0 mmol/L)</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>2-h PG &gt;200 mg/dL (11.1 mmol/L) during an OGTT</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>HbA1c &gt; 6.5%.</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>A random plasma glucose &gt;200 mg/dL(11.1 mmol/L)in a patient with classic symptoms of hyperglycaemia or hyperglycemic crisis.</td>
</tr>
</tbody>
</table>
3.3 Confirmation of diagnosis

Unless a clear clinical diagnosis (patient in a hyperglycaemic crisis or with classic symptoms of hyperglycaemia) is available, diagnosis should be confirmed by repeating the same test with a new blood sample or by another test. If the patient is having discordant results from two different tests, then the test result that is above the diagnostic cut off should be repeated (5-7)).

3.4 Prediabetes

There are some individuals whose plasma glucose levels are below the diagnostic level, but too high to be considered normal. They have impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT). This situation is referred to as prediabetes and it indicates a risk of developing diabetes in future. Diagnostic criteria of prediabetes are given in table 2.

<table>
<thead>
<tr>
<th>Table 2: Criteria for the diagnosis of prediabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>FPG 100 - 125 mg/dL (5.6 – 6.9 mmol/L)</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>2-h PG 140 -199 mg/dL (7.8-11.0 mmol/L) during an OGTT</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>HbA1c 5.6 -6.4%</td>
</tr>
</tbody>
</table>
4. SCREENING FOR TYPE 2 DIABETES

Screening can detect diabetes early and may prevent adverse outcomes. T2DM may remain undiagnosed for several years because patients usually do not develop symptoms of hyperglycaemia at earlier stages. Nevertheless, patients are at risk developing long-term complications by the time of diagnosis due to exposure to chronic hyperglycaemia.

4.1. Criteria of screening for type 2 diabetes (5-7)

- All adults aged more than 40 years
- All patients who are overweight or obese and have additional risk factors for T2DM (Table 3)
- If the initial screening test is normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results (e.g., patients with prediabetes should be tested yearly) and risk status (e.g. presence of multiple risk factors)

Table 3: Risk factors for Type 2 Diabetes, in addition to South Asian origin (5,6,7)

<table>
<thead>
<tr>
<th>Risk Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ Overweight and obese (BMI &gt; 23 kg/m2)</td>
</tr>
<tr>
<td>➢ Physical inactivity</td>
</tr>
<tr>
<td>➢ First-degree relative with type 2 diabetes</td>
</tr>
<tr>
<td>➢ History of gestational diabetes or a women who delivered a baby weighing &gt;3.5 kg</td>
</tr>
<tr>
<td>➢ History of pre diabetes (IGT or IFG or A1c 6.0 to 6.4%)</td>
</tr>
</tbody>
</table>
| ➢ Presence of CV risk factors  
  ➢ Hypertension (>140/90 mmHg or on therapy for hypertension)  
  ➢ HDL cholesterol level <35 mg/dl and/or a triglyceride level>250 mg/dl  
  ➢ Women with polycystic ovary syndrome |
| ➢ Other clinical conditions associated with insulin resistance (e.g. severe obesity, acanthosis nigricans) |
5. CLINICAL EVALUATION

A comprehensive clinical assessment should be carried out at the first encounter of a patient with diabetes. This would provide useful information in addressing the lifestyle, behavioural, dietary and pharmaceutical interventions that are the main goals in management of the disease. Detailed medical history, physical examination and laboratory investigations should be obtained during the initial clinical assessment (Table 4).

<table>
<thead>
<tr>
<th>Table 4: Clinical Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>History</strong></td>
</tr>
<tr>
<td>➢ Age of onset and details of first presentation e.g. asymptomatic, hyperglycaemic emergency, laboratory results</td>
</tr>
<tr>
<td>➢ Presence of other comorbidities: hypertension, dyslipidaemia, ischaemic heart disease, dental diseases</td>
</tr>
<tr>
<td>➢ Family history</td>
</tr>
<tr>
<td>➢ Psycho-social history</td>
</tr>
<tr>
<td>➢ Eating patterns, nutritional status</td>
</tr>
<tr>
<td>➢ History of smoking, alcohol consumption</td>
</tr>
<tr>
<td>➢ Review of previous treatment regimens management problems and complications</td>
</tr>
<tr>
<td>• Blood sugar records, HbA1C records</td>
</tr>
<tr>
<td>• Hyperglycaemic emergencies: frequency, severity, and cause</td>
</tr>
<tr>
<td>• Hypoglycemia episodes, awareness, and frequency and causes</td>
</tr>
<tr>
<td>• Microvascular complications: retinopathy, nephropathy, and neuropathy (sensory, autonomic including sexual dysfunction)</td>
</tr>
<tr>
<td>• Macrovascular complications: coronary heart disease, cerebrovascular disease, and peripheral vascular disease</td>
</tr>
<tr>
<td>• Patient’s attitudes and evidence of self management</td>
</tr>
<tr>
<td><strong>Physical Examination</strong></td>
</tr>
<tr>
<td>• Height, weight and BMI</td>
</tr>
<tr>
<td>• Acanthosis nigricans, insulin injection sites</td>
</tr>
<tr>
<td>• Blood pressure with postural measurements, peripheral pulsations esp. dorsalis pedis and posterior tibial pulses</td>
</tr>
<tr>
<td>• Fundoscopic examination</td>
</tr>
<tr>
<td>• Presence/absence of ankle reflexes, sensations including pain, proprioception, vibration, and monofilament sensation</td>
</tr>
</tbody>
</table>
Investigations
- Fasting lipid profile
- Serum creatinine and estimated GFR
- Urine albumin-creatinine ratio
- Thyroid function test in T1DM, dyslipidaemia
- HbA1C if not done during past 3 months

6. MANAGEMENT OF TYPE 2 DIABETES MELLITUS

The main goals of management of Type 2 DM include,

1) Life style modification and patient education
2) Maintenance of good glycaemic control
3) Multiple risk factor management
4) Prevention of complications

This can be best achieved through a patient centered self-management approach with multidisciplinary support.

6.1. LIFE STYLE MODIFICATION & PATIENT EDUCATION

Life style modification is the key foundation for the better management of diabetes. Patient education is an essential continuous process to facilitate patient’s knowledge, skills and ability necessary for self-diabetes care.

- Medical nutrition therapy (5-7)
  - Should be individualized.
  - Weight loss is recommended (at least 5-10%) for all overweight or obese individuals with a calorie restricted diet. All patients should attempt to have near normal body weight (BMI – 18.5-23kg/m²)
  - Saturated fat and trans fat intake should be reduced.
  - Salt intake should be limited to less than 2.4 g sodium (i.e. 1 tea spoon of salt).
  (Refer Annexure for sample dietary plan for patient with diabetes)

- Physical activity
  - Increasing day to day physical activity is recommended as a more practical approach.
  - Moderate intensity aerobic physical activity (e.g. walking, cycling, swimming) is recommended.
At least 150 min/week (e.g. brisk walk 30 minutes a day 5 days a week).
- For obese patients at least 60 minutes of exercise per a day.
- Resistance training (e.g. pushups, dumbbells) is recommended at least twice a week.
- Encourage muscle-strengthening activities that involve all major muscle groups (2 or more days per week)

- **Smoking and Alcohol**
  - All patients should be encouraged to quit smoking.
  - Alcohol is best avoided. If taken it should be less than two units per day for men and less than one unit per day for women.

### 6.2. GLYCAEMIC CONTROL (5-11)

#### 6.2.1. Glycaemic Targets

Following optimal targets for glycaemic control is recommended (table 5), but each target must be individualized based on comorbid conditions, hypoglycemia unawareness, duration of diabetes, age, life expectancy, patient motivation and individual patient considerations (Figure 1). A higher glycemic target may be acceptable in elderly or those who are at risk of hypoglycaemia.

<table>
<thead>
<tr>
<th>Table 5: Glycaemic Targets</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c</td>
</tr>
<tr>
<td>FPG/ Pre-prandial capillary plasma glucose</td>
</tr>
<tr>
<td>Post prandial plasma glucose/ Peak post-prandial capillary plasma glucose <em>(1-2 hrs after the beginning of a meal)</em></td>
</tr>
</tbody>
</table>

Figure 1: Individualized Glycaemic targets
6.2.2. Monitoring of glycaemic control

- Ideally a combination of HbA1c and self-monitoring of capillary glucose will give optimal results.
- Fasting plasma glucose and post-prandial plasma glucose are commonly used for assessment of glycaemic control in our setting due to lack of facilities for above tests.
- If HbA1c goal is not achieved despite normal fasting/pre-prandial blood sugar target, the post prandial blood glucose should be targeted.
- When the HbA1c level does not correlate with plasma glucose levels, conditions that affect red cell turn over such as anaemia, haemorrhage or haemoglobinopaties should be considered.

6.3. PHARMACOTHERAPY

6.3.1. Initiation of pharmacotherapy (Figure 2)

- At initial diagnosis, monotherapy with metformin (unless contraindicated) along with lifestyle interventions is the preferred choice as most patients cannot achieve recommended targets on lifestyle interventions alone.
- In the presence of moderate to severe hyperglycaemia at diagnosis, dual/triple therapy or insulin may be considered.
- Insulin therapy may be required if there are severe symptoms or complications at presentation. Once the hyperglycaemia is controlled, changing over to non-insulin therapies may be possible.
- Consider timely initiation of combination therapy if monotherapy appears inadequate. The combined regimen should aim for good glycaemic efficacy, low potential for hypoglycaemia as well as weight neutrality or ideally weight loss in the obese and cost effectiveness.
- Sulphonylurea is used as the second line treatment option or as the first choice in metformin intolerant/contraindicated patients in local setting due to absence of robust data on superiority of other agents, low cost and availability.
- Nevertheless, any combination of anti hyperglycaemic agents such as sulfonylurea, thiazolidinedione, DPP-4 inhibitors, SGLT2 inhibitors, GLP-1 receptor agonists, or insulin can be considered for the combination therapy.
**Figure 2: ALGORITHM FOR GLUCOSE LOWERING IN TYPE 2 DM**

Lifestyle modification +
Metformin (unless contraindicated or not tolerated)

Glycaemic target not achieved in 3 months

**Add a second agent**
Sulfonylurea*(preferred due to efficacy, availability & low cost)*
Or DPP4 Inhibitor
Or Alpha glucosidase inhibitors
Or GLP-1 RA
Or SGLT2 inhibitor
Or TZD
Or Glitanides
Or Basal Insulin

Glycaemic target not achieved in 3 months

**Add a third agent**
Sulfonylurea
Or DPP4 Inhibitor
Or Alpha glucosidase inhibitors
Or Glitanides
Or GLP-1 RA
Or SGLT2 inhibitor
Or TZD
Or Basal insulin

Glycaemic target not achieved in 3-6 months

Complex insulin regimen with multiple daily doses
6.3.2. Non insulin therapies for T2DM

Brief introduction to available glucose lowering agents are given below. Refer to table 6 for dosages and adverse effects.

**Biguanides: Metformin**

- Metformin is the drug recommended for initial monotherapy for patients with T2DM.
- Metformin decreases hepatic gluconeogenesis, decreases intestinal absorption of glucose and improves insulin sensitivity by increasing peripheral uptake and utilization of glucose.
- Metformin can be safely used down to glomerular filtration rate (GFR) of 45 mL/min/1.73 m$^2$. It should be used with caution at eGFR 45-30 mL/min/1.73 m$^2$ with a reduced dosage.

**Sulphonylureas (SU): Tolbutamide, Glibenclamide, Gliclazide, Glimipride & Glipizide**

- Sulfonylureas are insulin secretogogues (stimulate insulin secretion from the pancreatic beta-cells) with well established glucose lowering efficacy and safety.
- Individual SUs differ in their hypoglycaemic potential. Gliclazide and Glimipride has shown low hypoglycaemic events, while Glibenclamide is known to have high risk for hypoglycaemia especially in elderly.
- SUs are linked to weight gain due to its insulinotrophic effects. But modern agents such as Glimipride, Gliclazide MR(Modified release), Glipizide ER(extended release) have shown weight neutralizing/ reducing effects.

**Alpha glucosidase inhibitors: Acarbose**

- This drug acts by reducing post prandial glucose excursions by inhibiting gut carbohydrate digestion. This is taken before meals.

**Thiazolidinediones (TZD): Pioglitazone**

- Pioglitazone is the only TZD used in Sri Lanka. It is known to improve insulin sensitivity in T2DM.
- Its clinical use has become limited by the risk profile, including weight gain, worsening heart failure, macular oedema, increased fracture risk and possible risk for bladder cancer.
**Dipeptidyl peptidase-4 inhibitor (DPP4 Inhibitors):**

Sitagliptin, Vildagliptin, Saxagliptin, Linagliptin, Alogliptin

- DPP4 inhibitors are a group of incretin based therapy available for treatment of DM.
- It is weight neutral and does not cause hypoglycaemia, unless used in combination with SU or insulin.

**Sodium glucose co-transporter inhibitors (SGLT2 inhibitors)**

Empagliflozin, Dapagliflozin, Canagliflozin

- SGLT2 inhibitors block the renal glucose reabsorption and causes glycosuria resulting in its glucose lowering effect.
- Hypoglycaemia is not a significant adverse effect. Urinary tract infections and vaginal candidiasis has been commonly associated with this class of drugs.

**Glucagon-like peptide-1 (GLP-1) receptor agonists:**

Exenatide, Liraglutide, Exenatide modified release, Albiglutide, Dulaglutide

- This is a group of injectable therapy in incretin family. These are generally well tolerated, with transient mild to moderate gastrointestinal side effects at the introduction of the drug.
- Weight loss has been shown in dose-dependent manner. No hypoglycaemic events are seen, unless in combination with other therapies. These drugs are injectable and costly.

### Table 6: Non-insulin therapies for Type 2 DM

<table>
<thead>
<tr>
<th>Class /compound</th>
<th>Dose</th>
<th>Advantage</th>
<th>Disadvantage</th>
<th>Reduction of HbA1c</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Biguanides</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Metformin</strong></td>
<td>500-2000mg in divided doses</td>
<td>Extensive experience</td>
<td>GI side effects (diarrhoea, abdominal cramps)</td>
<td>1-2%</td>
</tr>
<tr>
<td></td>
<td>Start at a low dose after meals</td>
<td>No weight gain</td>
<td>Lactic acidosis risk (extremely rare)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>No hypoglycaemia</td>
<td>Vitamin B12 deficiency (rare)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Likely ↓ CVD events</td>
<td>Multiple contraindications: CKD, acidosis, hypoxia, dehydration</td>
<td></td>
</tr>
<tr>
<td><strong>Sulfonylureas</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Tolbutamide</strong></td>
<td>500-2000mg in divided doses</td>
<td>Extensive experience</td>
<td>Hypoglycaemia</td>
<td>1-2%</td>
</tr>
<tr>
<td></td>
<td>40-320mg in 1-3 divided doses</td>
<td>No weight gain</td>
<td>Weight gain</td>
<td></td>
</tr>
<tr>
<td></td>
<td>30-120mg daily</td>
<td>No hypoglycaemia</td>
<td>?Glibenclamide, Tolbutamide may blunt myocardial ischemic preconditioning</td>
<td></td>
</tr>
<tr>
<td><strong>Gliclazide</strong></td>
<td></td>
<td>Extensive experience</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>40-320mg in 1-3 divided doses</td>
<td>↓ Microvascular risk</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gliclazide MR</strong></td>
<td>30-120mg daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug Class</td>
<td>Drug Name</td>
<td>Dosage/Route</td>
<td>Side Effects</td>
<td>Notes</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>--------------------</td>
<td>-------------------------------------</td>
<td>-----------------------------------------------------------------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td>Glitazones</td>
<td>Glipizide</td>
<td>2.5-20mg in divided doses</td>
<td>No hypoglycaemia</td>
<td>Low durability</td>
</tr>
<tr>
<td></td>
<td>Glibenclamide</td>
<td>2.5-15mg daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Glimepiride</td>
<td>1-6mg daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long-acting α-glucosidase inhibitor</td>
<td>Acarbose</td>
<td>150-600mg in divided doses before meals</td>
<td>Gastrointestinal side effects (flatulence, diarrhoea)</td>
<td>0.5-1%</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>Repaglinide</td>
<td>0.4-4mg 60-180mg with meals</td>
<td>↑Insulin secretion</td>
<td>Gastrointestinal side effects</td>
</tr>
<tr>
<td></td>
<td>Nateglinide</td>
<td>50mg twice daily 5mg daily</td>
<td>Controls postprandial hyperglycaemia, Less weight gain in obese</td>
<td></td>
</tr>
<tr>
<td>DPP-4 inhibitors</td>
<td>Sitagliptin</td>
<td>50 - 100mg once daily</td>
<td>No hypoglycaemia</td>
<td>Generally modest HbA1c reduction and efficacy</td>
</tr>
<tr>
<td></td>
<td>Vildagliptin</td>
<td>50mg twice daily 5mg daily</td>
<td>Well tolerated</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Saxagliptin</td>
<td>5mg daily</td>
<td>Weight neutral</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Linagliptin</td>
<td>5mg daily</td>
<td>CVD risk neutral</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Alogliptin</td>
<td>6.25- 25mg daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GLP1 receptor agonists</td>
<td>Exenatide twice daily</td>
<td>5-10µg twice a day 0.6-1.8mg daily 2mg once weekly 30-50mg weekly 0.75-1.5mg weekly 20µg once daily 2.5-40mg daily</td>
<td>No hypoglycaemia Weight reduction ? Potential for improved β-cell mass/function Cardiovascular benefit (semaglutide/ liraglutide)</td>
<td>Gastrointestinal side effects (nausea/vomiting) C-cell hyperplasia/medullary thyroidtumours in animals Injectable Training requirements</td>
</tr>
<tr>
<td></td>
<td>Liraglutide</td>
<td>50mg twice daily 5mg daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exenatide modified release</td>
<td>2mg once weekly 30-50mg weekly</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Albiglutide</td>
<td>0.75-1.5mg weekly 20µg once daily 2.5-40mg daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dulaglutide</td>
<td>50mg twice daily 5mg daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lixisenatide</td>
<td>15-30mg once daily</td>
<td>No hypoglycaemia</td>
<td>Weight gain Oedema/heart failure Fractures ? ↑ Bladder cancer</td>
</tr>
<tr>
<td></td>
<td>Semaglutide</td>
<td>50mg twice daily 5mg daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TZD</td>
<td>Pioglitazone</td>
<td>5-10mg once daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>with/without meals 100-300mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SGLT2 Inhibitor</td>
<td>Dapagliflozin</td>
<td>5-10mg once daily</td>
<td>No hypoglycaemia</td>
<td>Increased Genitourinary infections Polyuria Euglycaemic ketoacidosis Volume depletion/</td>
</tr>
<tr>
<td></td>
<td>Canagliflozin</td>
<td>5-10mg once daily</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
6.3.3. Sequential insulin strategy in Type 2 DM (Figure 3)

- T2DM is a progressive disease and with time OHA may fail to achieve glycaemic targets. Insulin therapy should be promptly started in such patients.

- Basal insulin (Insulin Glargine, Detemir, Isophane insulin) is recommended as add on therapy to OHAs, starting at 6-10 units or 0.1 -0.2 units/kg at bedtime. It can be adjusted by 2-4 units once or twice weekly to achieve the desired FBS. Long acting basal insulin analogues (Glargine and Detemir) have a lower risk of hypoglycaemia, but these are expensive. Intermediate acting Isophane insulin is a cheaper alternative in the local setting.

- If the post-prandial glucose (>180mg/dl) and HbA1c remains high, despite high doses of basal insulin (>0.5-1U/kg), consider adding one dose of pre-meal regular or rapid acting insulin. Premixed insulin (twice daily) either alone or in combination with OHAs can be used as an alternative regimen at this point.

- In patients who do not meet the glycaemic targets with above insulin regimens “basal-bolus” insulin therapy should be considered. Basal bolus therapy involves giving longer acting insulin during fasting state to keep the basal plasma glucose stable and giving pre meal shorter acting insulin to control the post prandial rise of plasma glucose. It is preferable to refer such patients to a diabetic clinic for advice by a specialist.

- Refer to annexure 2 for details of insulin types

<table>
<thead>
<tr>
<th>Empagliflozin</th>
<th>daily</th>
<th>stages of T2DM &amp; T1DM</th>
<th>Hypotension/ Dizziness</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 - 25mg daily</td>
<td>Better cardiovascular outcome (Empagliflozin)</td>
<td>↑LDL</td>
<td>↑creatinine transiently</td>
</tr>
</tbody>
</table>
Figure 3: SEQUENTIAL INSULIN STRATEGY IN TYPE 2 DM

Non insulin regimen

Add Basal insulin (Isophane or long acting insulin analogue daily at bed time)

Start with 0.1-0.2U/kg or 6-10U

Adjust by 10-15% or 2-4 U once-twice weekly to achieve the desired FBS

Post prandial glucose >180mg/dl
HbA1c remains high despite normal FBS
Basal insulin dose >0.5-1U/kg

Glycaemic targets are not achieved

Basal insulin + 1 meal time short/rapid acting insulin

Pre-mixed insulin Twice a day

Basal bolus insulin regimen
Basal insulin plus pre meal short/rapid acting insulin
6.4. PRINCIPLES OF MANAGEMENT OF PREDIABETES

- Intensive life style measures targeting weight loss of 7% of body weight significantly reduces CV risk and development of overt diabetes.
- Metformin may be considered especially for obese (BMI > 35 kg/m²), young people (less than 60 years) and women with a history of gestational diabetes.
- Annual monitoring for the development of diabetes is recommended.
- Screening and treatment of modifiable risk factors for cardiovascular disease should be done.

6.5. MANAGEMENT OF DIABETES IN ELDERLY

- An HbA1c goal of 7-8% is adequate in most elderly and a less stringent control is recommended for those with shorter life expectancy.

- Drugs should be started at the lowest dose and titrated up gradually.

- Polypharmacy may affect compliance, cause drug interactions and worsen adverse effects such as hypoglycaemia and hypotension.

<table>
<thead>
<tr>
<th>Table 7: Glycaemic recommendations for Older Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient characteristics</td>
</tr>
<tr>
<td>--------------------------</td>
</tr>
<tr>
<td>Healthy</td>
</tr>
<tr>
<td>Complex/Intermediate</td>
</tr>
<tr>
<td>Very complex/poor health</td>
</tr>
</tbody>
</table>
7. MANAGEMENT OF CARDIOVASCULAR RISK FACTORS (5-7, 12-17)

Cardiovascular diseases (CVD) are the major cause of morbidity and mortality among diabetic patients; two thirds of diabetics die of cardiovascular diseases. CVD are defined as coronary artery disease (CAD) which include myocardial infarction, stable or unstable angina and coronary revascularization, stroke, transient ischaemic attack and atherosclerotic peripheral vascular disease.

Diabetes itself is considered as a independent risk factor for CV disease. Furthermore, majority of patients with diabetes has additional cardiovascular risk factors (Table 8). Presence of additional CV risk factors exponentially increases cardiovascular morbidity and mortality.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>History of current and past smoking habits/ exposure to passive smoking</td>
</tr>
<tr>
<td>Hypertension</td>
<td>History of hypertension on therapy</td>
</tr>
<tr>
<td></td>
<td>Blood pressure &gt;140/90mmHg</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>LDL cholesterol &gt;100 mg/dL (2.6 mmol/L)</td>
</tr>
<tr>
<td>Albuminuria/ microalbuminuria</td>
<td>UACR (&gt;30mg/g) with otherwise normal UFR</td>
</tr>
<tr>
<td>Family history of premature cardiovascular disease</td>
<td>CVD in first-degree male relatives &lt; 55 years or female relatives &lt; 65 years.</td>
</tr>
<tr>
<td>Established Coronary artery disease</td>
<td>History of ischaemic heart disease</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>History of stroke or transient ischaemic attacks</td>
</tr>
<tr>
<td>Chronic Kidney disease</td>
<td>abnormalities of kidney structure or function (eGFR &lt; 60ml/min/1.73m²), present for &gt;3 months, with implications for health</td>
</tr>
</tbody>
</table>

We recommend that all patients should be evaluated for CV risk factors at the diagnosis of diabetes and annually thereafter.
Figure 4: Algorithm for management of CV risk in Diabetes

CVD risk assessment for all adult Diabetic patients at diagnosis

Assess for established CVD

No established CVD

CVD risk factor Assessment
Look for the presence of
- Hypertension
- Dyslipidemia
- Cigarette smoking
- Obesity
- Physical inactivity
- Albuminuria
- Family history of premature CVD

Control modifiable risk factors

Diagnosed CAD

Secondary prevention
- Life style modification
- Antiplatelet
- Statin (high intensity)
- Control other modifiable risk factors

Cardiology referral

Symptoms of CAD or Abnormal routine ECG

Asymptomatic for CAD and Normal routine ECG

Manage according to the CVD risk. Screening for CAD not needed

No statin therapy

Annual risk Factor assessment

If CVD risk >10% or age > 50years with an additional risk factor

Add a statin irrespective of LDL

Start Aspirin
7.1. Blood pressure control

Good blood pressure control has proven to be beneficial in reducing complications of diabetes mellitus. Blood pressure should be recorded at the time of diagnosis and every routine visit. BP measurement should be carried out according to established guidelines (Ref to Hypertension management guidelines, CCP)

- Diabetic patients with office BP > 140/90 mmHg should be treated with lifestyle measures and pharmacological therapy to achieve target BP less than 140/90 mmHg.
- Lower BP targets of <130/80 mmHg can be considered for younger patients, patients with albuminuria and/or chronic kidney disease.
- In older adults lowering blood pressure to <130/70 mmHg is not recommended.

**Pharmacological therapy**

- Drug of first choice is an angiotensin converting enzyme inhibitor (ACEi). Angiotensin receptor blocker (ARB) can be used where ACEi is not tolerated.
- A combination of drug classes (ACEI/ARB plus CCB, thiazide diuretic, beta blockers, alfa-blockers) may be necessary to achieve the blood pressure targets.
- Combination of ACEi and ARB together is not recommended due to increased incidence of hyperkalaemia and renal impairment.
7.2. Management of dyslipidaemia in diabetes

- Intensification of life style modifications addressing weight loss, dietary advice and physical activity is recommended as the initial step.
- Statin is the drug of choice to lower LDL cholesterol and to reduce the risk of CV disease. ADA Standard of Care position statement 2017 (revised) recommends high vs. moderate intensity statin therapy (Table 9) based on risk factor profile.
- Cardiovascular risk factors include LDL cholesterol $\geq$100mg/dl, high blood pressure, smoking, obesity and family history of premature CV disease.

<table>
<thead>
<tr>
<th>Table 9: High and moderate intensity Statin therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate intensity</td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td><strong>Lowers LDL cholesterol by 30% to&lt;50%</strong></td>
</tr>
<tr>
<td>Atorvastatin 10 -20 mg</td>
</tr>
<tr>
<td>Rosuvastatin 5- 10 mg</td>
</tr>
<tr>
<td>Simvastatin 20 – 40 mg</td>
</tr>
<tr>
<td>Pravastatin 40 – 80 mg</td>
</tr>
</tbody>
</table>

7.2.1. Recommendations for statins based on cardiovascular risk in people with diabetes

**Age less than 40 years**

- Statin therapy is not recommended for individuals with no risk factors.
- Moderate intensity statin therapy is recommended for those with other CV risk factors.
- For those who have established cardiovascular disease high intensity statin therapy is recommended.

**Age - 40-75 years**

- All patients even without additional risk factors will need moderate intensity statin therapy.
- Patients with cardiovascular risk factors and/or established cardiovascular disease should be given high intensity statin therapy.
Age >75years

- Limited data are available on the benefit of statin therapy in this age group. Therefore statin therapy should be individualized depending on risks and benefits.
- Individualized decision should be made in those without CV risk factors.

7.2.2. Other lipid lowering therapies

- For patients with fasting triglyceride levels >500 mg/dL (5.7 mmol/L), evaluate for secondary causes and consider medical therapy with fibrates to reduce risk of pancreatitis.
- Addition of ezetimibe to moderate-intensity statin therapy can be considered in
  - high risk patients who have less than anticipated response to statins
  - Patients unable to tolerate the recommended intensity of a statin
- Combination therapy of statins with fibrates (gemfibrozil, fenofibrate) is not shown to significantly reduce the CV outcome (11) but associated with higher incidence of side effects; elevated transaminases myositis and rhabdomyolysis.

7.2.3. Follow up for lipid lowering therapy

- Lipid profile should be obtained at the time of diagnosis and any time before initiation of statin therapy. Follow up lipid profile may be helpful in monitoring compliance. However it is not always necessary once the patient is stable on therapy.
- There is no evidence to support titrating doses to achieve optimal LDL and HDL in both primary and secondary prevention of CVD.

7.2.4. Antiplatelet therapy

- Low dose aspirin therapy (75mg/day) is recommended for primary prevention of CV disease in individuals with diabetes if they have a 10-year risk of CV events over 10%.
- This will include most men and women aged 50 years or above with one or more of the major risk factors which include,
  - Smoking
- Hypertension
- Dyslipidaemia
- Family history of premature coronary artery disease
- Albuminuria

- Aspirin therapy is indicated as secondary prophylaxis for those with established cardiovascular disease.

8. MANAGEMENT OF COMPLICATIONS OF DIABETES MELLITUS (5-7, 17-25)

Tight glycaemic control from early stages of diabetes, is known to prevent and delay the progression of microvascular and macrovascular complications. Apart from glycaemic control, other factors such as adequate blood pressure control, lipid control and stopping smoking are also important in preventing complications.

Screening for microvascular complications in Type 2 DM should be started at diagnosis. Screening in type1 diabetes should be initiated after 5 years from the diagnosis. Once started, screening should be repeated at least annually.

8.1. Diabetic Neuropathy

8.1.1. Distal Symmetrical polyneuropathy (DPN)

- Assessment of DPN should include a careful history and 10-g monofilament testing with at least one of the following tests: pinprick sensation, ankle reflex or vibration perception using 128 Hz tuning fork, vibration perception threshold (using the Bio-Thesiometer)
- DPN is a diagnosis of exclusion. In all patients with diabetes and peripheral neuropathy, causes of neuropathy other than diabetes should be considered. They include, toxins, alcohol, vitamin B12 deficiency, hypothyroidism, renal disease, CIDP, malignancies (multiple myeloma, bronchogenic carcinoma), infections (leprosy, HIV), vasculitis and drugs. An alternative cause is suggested by the presence of asymmetry, high ESR, absence of other microvascular complications and rapid progression.
• Presence of peripheral neuropathy in a diabetic is a major risk factor for foot complications. Therefore, emphasis should be made on proper foot care.
• Optimal glucose control will delay the progression of DPN.
• Painful DPN is treated with the following symptomatic therapy,
  ▪ Antidepressants - TCA, SNRI
  ▪ Antiepileptics – pregabalin, gabapentin, phenytoin, carbamazepine
  ▪ Topical Capsacin

8.1.2. Diabetic autonomic neuropathy

Major clinical manifestations of diabetic autonomic neuropathy are resting tachycardia, exercise intolerance, orthostatic hypotension, gastroparesis, constipation, erectile dysfunction and lack of autonomic response to hypoglycaemia.

Management of Diabetic autonomic neuropathy

• Gastroparesis
  ▪ Dietary modifications: Low fat low fiber diet
  ▪ Prokinetic drugs: Metoclopramide, Domperidone, Erythromycin
  ▪ Others: NG drainage, Intra jejunal feeding, gastric pacemaker therapy
  ▪ Due to side effects with long term use of metoclopramide, it should be reserved for patients with most severe symptoms unresponsive to other therapies and the duration of therapy should not exceed three months.

• Autonomic Diarrhea
  ▪ Codeine, Loperamide, Antibiotics, Clonidine

• Erectile dysfunction
  ▪ Phosphodiesterase inhibitors: Sildenafil, Tadalafil
  ▪ Prostaglandins: Alprostadil
  ▪ Vacuum devices and prosthesis

• Postural hypotension
  ▪ Non pharmacological: adequate salt intake, compressive garments over the legs and abdomen, avoiding medications that aggravate hypotension, standing slowly from lying down position.
- Pharmacological: fludrocortisone, Midodrine

### 8.2. Diabetic foot Complications

Follow up and management of diabetic foot depends on the risk category, categorized according to the presence of the following four risk factors (table 10).

- Previous ulcer or amputation
- Peripheral Artery Disease
- Current deformity /callus/ulcer
- Sensory neuropathy (see section on neuropathy assessment)

| Table 10: Management of Diabetic foot complications |
|---------------------------------|-----------------|---------------------------------|
| Risk category                  | Definition                                      | Recommended action               | Review          |
| Low Risk foot                  | No risk factors                                   | Foot care education              | Annual          |
|                                |                                               | Optimize metabolic control       |                 |
| High risk foot                 | 1 risk factor present                           | Special foot wear                | Every 3 -6 months |
|                                |                                               | Offer intervention               |                 |
|                                |                                               | Above Measures                   |                 |
| Super high risk foot           | Previous ulceration or                          | Special foot wear                | Every 2 -3 months |
|                                | amputation or                                    | Offer intervention               |                 |
|                                | 2 of other risk factors                         | Above Measures                   |                 |
| Foot emergencies               | Ulcer                                         | Offer treatment                  | Every 1 -2 months |
|                                | Injury                                         | appropriately.                   |                 |
|                                | Infection                                      | Above Measures                   |                 |

Foot care advices and patient motivation should be done regularly.

Foot care advices include,

- Use of appropriate footwear
- Avoid walking barefoot
- Keeping feet clean and dry. Application of moisturizer to prevent cracked soles
- Trimming toe nails appropriately
- Inspection of feet for early detection of complications such as infection, blisters and callus
In the presence of neuropathic ulcer and charcot foot, refer for offloading with appropriate footwear or casts.

8.3. Peripheral Arterial disease (PAD)

PAD is a marker of systemic vascular disease (MI, Stroke). A significant proportion of patients with PAD are asymptomatic.

8.3.1. Assessment of PAD

- Obtain history of claudication, rest pain.
- Examine the extremity for pulse, non-healing wounds and gangrene
- Ankle- Brachial index (ABI) is indicated in the following circumstances
  - Clinical PAD
  - Age> 50 years or < 50 years with other PAD risk factors
    (e.g: smoking, hypertension, hyperlipidemia)
- ABI may be falsely negative in calcified-poorly compressible vessels associated with diabetes and advanced age and in moderate aortoiliac stenosis
- The diagnostic criteria for PAD based on the ABI are as follows
  - Normal if 0.91–1.30
  - Mild obstruction if 0.70–0.90
  - Moderate obstruction if 0.40–0.69
  - Severe obstruction if <0.40
  - Poorly compressible if >1.30

8.3.2. Management of PAD

- Foot care advice
- Cessation of smoking
- Optimize cardiovascular risk factors
- Exercise rehabilitation-supervised treadmill walking
- Drugs – Cilostazol
- Revascularization in
- Refractory claudication
- Critical limb Ischaemia rest pain or tissue loss-non-healing ulcer/gangrene)

(Revascularization is not indicated in individuals with severe reduction in ABI <0.4 in the absence of symptoms)

8.4. Diabetic Nephropathy

- Onset and progression of nephropathy should be assessed by,
  - Spot urinary albumin to creatinine ratio -preferably in the first void sample
  - Serum creatinine with Estimated glomerular filtration rate (eGFR)

- Marked hyperglycaemia, very high blood pressure, excessive physical exercise in the previous 24 hours, urinary tract infection, fever, congestive heart failure are known to cause transient elevations in urinary albumin excretion.
- Persistent albuminuria is defined as albumin to creatinine ratio ≥ 30 mg/g continuing over 3-6 months. Treatment of persistent albuminuria retards progression to ESRD.
- In patients with renal impairment consider and exclude alternative causes (Table 11)

**Table 11 : Situations where an alternative cause of renal impairment should be considered**

- Absence of retinopathy
- Presence of active urine sediments
- Rapidly increasing proteinuria
- Rapidly decreasing eGFR
- Evidence of systemic diseases-vasculitis
- Evidence of urological cause -Abnormal findings on renal ultrasound
- Resistant hypertension
- > 30% reduction in eGFR after initiating ACE inhibitor or ARB therapy

8.4.1. Management of diabetic nephropathy

- Maintaining normoglycaemia is shown to delay the onset and progression of diabetic nephropathy in both Type 1 DM and Type 2 DM.
• Blood pressure targets of <140/90 mmHg (if albuminuria, < 130/80 mmHg) is recommended to retard the progression of CKD. Either ACEI or ARB (in patients intolerant to ACEi) is recommended for management of albuminuria even in normotensive patients and for blood pressure reduction. Combination therapy with ACEI and ARB is not recommended.

• When eGFR is below 60 ml/min/1.73 m², potential complications of CKD should be evaluated and managed (Table 12). These patients are best managed under specialist care.

<table>
<thead>
<tr>
<th>eGFR (mL/min/1.73 m²)</th>
<th>Management</th>
</tr>
</thead>
</table>
| 45–60                | • Monitor eGFR 6 monthly  
                      • Monitor electrolytes, bicarbonate, hemoglobin, calcium, phosphorus and parathyroid hormone yearly  
                      • Assure vitamin D sufficiency.  
                      • Consider bone density testing |
| 30–44                | • eGFR every 3 months  
                      • Monitor electrolytes, bicarbonate, calcium, phosphorus, parathyroid hormone, hemoglobin, albumin and weight every 3–6 months.  
                      • Consider the need for dose adjustment of medications.  
                      • Assure vitamin D sufficiency  
                      • Consider bone density testing |
| <30                  | • Referral to a Nephrologist |

8.5. Diabetic Retinopathy

The local prevalence of diabetic retinopathy in diagnosed patients with diabetes was found to be 27% (93.4% NPDR, 5.3% maculopathy).

Risk factors for progression of retinopathy

• Duration of diabetes
• Chronic hyperglycaemia
• High blood pressure
• Renal disease
8.5.1. Screening and management of Diabetic Retinopathy

- All patients with type 2 diabetes should be screened for diabetic retinopathy at the time of diagnosis with direct ophthalmoscopy/ slit lamp and fundus lens/ mydriatic or non mydriatic fundus photography
- Management, specialist referral and follow up should be decided upon the presence and severity of diabetic retinopathy (table 13).

<table>
<thead>
<tr>
<th>Stage of Retinopathy</th>
<th>Features</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild non-proliferative</td>
<td>Microaneurysms</td>
<td>Control risk factors</td>
</tr>
<tr>
<td></td>
<td>Cotton wool spots &lt;5</td>
<td></td>
</tr>
<tr>
<td>Severe non-proliferative</td>
<td>Increased microaneurysms</td>
<td>Urgent ophthalmology referral</td>
</tr>
<tr>
<td></td>
<td>Multiple hemorrhages</td>
<td>Control risk factors</td>
</tr>
<tr>
<td></td>
<td>Cotton wool spots &gt; 5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Venous beading</td>
<td></td>
</tr>
<tr>
<td>Proliferative</td>
<td>New vessels and fibrous proliferation</td>
<td>Urgent ophthalmology referral-panretinal</td>
</tr>
<tr>
<td></td>
<td>Hemorrhages</td>
<td>photocoagulation, vitreoretinal surgeries</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Control risk factors</td>
</tr>
<tr>
<td>Advanced diabetic eye disease</td>
<td>Retinal detachment</td>
<td>Urgent ophthalmology referral-vitreoretinal</td>
</tr>
<tr>
<td></td>
<td>Rubeosis iris</td>
<td>surgeries</td>
</tr>
<tr>
<td></td>
<td>Neovascular glaucoma</td>
<td>Control risk factors</td>
</tr>
<tr>
<td>Maculopathy</td>
<td>Macular edema</td>
<td>Urgent ophthalmology referral-Focal Laser</td>
</tr>
<tr>
<td></td>
<td>Ischemic maculopathy</td>
<td>photocoagulation , VEGF antibody</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Control risk factors</td>
</tr>
</tbody>
</table>

- Women with preexisting diabetes who are planning pregnancy, should have a detailed eye examination. Laser photocoagulation minimizes the risk of progression of retinopathy during pregnancy.
- Those who have become pregnant, should be examined in the first trimester with close follow-up throughout pregnancy up to 1 year postpartum
9. MANAGEMENT OF DIABETIC EMERGENCIES (5-7, 26)

9.1. Diabetes ketoacidosis

Diabetic ketoacidosis (DKA) is an acute life-threatening complication of diabetes. It occurs mainly in patients with Type 1 DM. However, DKA can complicate Type 2 DM as well. DKA is a complex disorder of metabolic state characterized by hyperglycaemia, ketoacidosis, and ketonuria due to relative or absolute insulin deficiency.

9.1.1. Diagnosis of DKA

- Ketonaemia > 3.0 mmol/L or significant ketonuria (more than 2+ on standard urine sticks)
- Blood glucose > 11.0mmol/L or known diabetes mellitus
- Bicarbonate < 15.0mmol/L and/or venous pH < 7.3

9.1.2. Assessment of severity

The presence of one or more of the following may indicate severe DKA and should be reviewed by specialist and considered for referral to a HDU (High Dependency Unit) care

- Bicarbonate level below 5 mmol/L
- Venous/arterial pH below 7.0
- Blood ketones over 6 mmol/L
- Hypokalaemia on admission (under 3.5mmol/L)
- GCS less than 12
- Oxygen saturation below 92% on air (assuming normal baseline respiratory function)
- Systolic BP below 90mmHg
- Pulse over 100 or below 60bpm
- Anion gap above 16 \( \text{Anion Gap} = (\text{Na}^+ + \text{K}^+) - (\text{Cl}^- + \text{HCO}_3^-) \)

9.1.3. Management of DKA

9.1.3.1. Fluid replacement

Assess the severity of dehydration clinically by pulse and blood pressure. If systolic BP (SBP) on admission is below 90mmHg consider other causes of low blood pressure such as cardiogenic shock and sepsis in addition to hypovolemia.

- Give 500ml of 0.9% sodium chloride solution over 10-15 minutes.
- If SBP remains below 90mmHg this can be repeated
- If there has been no clinical improvement reconsider other causes of hypotension and seek an immediate specialized assessment
- Once SBP above 90mmHg continue fluid replacement as shown in Table 14.
Table 14. Fluid replacement regimen for a previously well 70kg adult

<table>
<thead>
<tr>
<th>Fluid</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.9% sodium chloride 1L *</td>
<td>1000 ml over 1st hour</td>
</tr>
<tr>
<td>0.9% sodium chloride 1L with KCl</td>
<td>1000 ml over next 2 hours</td>
</tr>
<tr>
<td>0.9% sodium chloride 1L with KCl</td>
<td>1000 ml over next 2 hours</td>
</tr>
<tr>
<td>0.9% sodium chloride 1L with KCl</td>
<td>1000 ml over next 4 hours</td>
</tr>
<tr>
<td>0.9% sodium chloride 1L with KCl</td>
<td>1000 ml over next 4 hours</td>
</tr>
<tr>
<td>0.9% sodium chloride 1L with potassium chloride</td>
<td>1000 ml over next 6 hours</td>
</tr>
</tbody>
</table>

Re-assessment of cardiovascular status at 12 hours is mandatory, further fluid may be required. A slower infusion rate should be considered according to age and other risk factors.

* Potassium chloride may be required if more than 1 liter of sodium chloride has been given already to resuscitate hypotensive patients.

Exercise caution and use central venous pressure measurements where possible to guide the rate of fluid administration in following groups of patients:

- Young adults aged <25 years
- Elderly
- Pregnant
- Heart or kidney failure
- Other serious co-morbidities

When blood glucose falls below 250 mg/dl (14.0 mmol/L), commence 10% glucose given at 125ml/hour alongside the 0.9% sodium chloride solution.

9.1.3.2. Insulin therapy

Intravenous insulin infusion of 0.1 units/per kilogram body weight is recommended.

Monitor capillary blood glucose hourly.

Metabolic treatment targets:

- Reduction of the blood ketone concentration by 0.5mmol/L/hour
- Increase the venous bicarbonate by 3.0mmol/L/hour
- Reduce capillary blood glucose by 3.0mmol/L/hour
- Maintain potassium between 4.0 and 5.5mmol/L

If these rates are not achieved, then the rate of insulin infusion should be increased.
Continue insulin infusion until the ketone measurement is less than 0.6mmol/L, venous pH over 7.3 and/or venous bicarbonate over 18mmol/L (Resolution of DKA)

**9.1.3.3. Potassium replacement**

Although DKA patients may present with hyperkalemia, with treatment (Fluid and insulin) potassium level falls. Table 15 will give a guide to potassium replacement.

<table>
<thead>
<tr>
<th>Potassium level (mmol/L)</th>
<th>Potassium replacement in mmol/L of infusion solution (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over 5.5</td>
<td>Nil</td>
</tr>
<tr>
<td>3.5-5.5</td>
<td>40</td>
</tr>
<tr>
<td>&lt;3.5</td>
<td>Senior review as additional potassium may be needed.</td>
</tr>
</tbody>
</table>

Monitor serum potassium 2 hourly and bicarbonate levels 2 hourly during the first six hours.

**9.1.3.4. Correction of acidosis**

Fluid and insulin replacement usually corrects acidosis. Bicarbonate administrations is potentially dangerous and not recommended.

**9.1.3.5. Assessment of resolution of ketoacidosis**

- Blood ketones less than 0.6mmol/L and
- Venous pH over 7.3 (do not use bicarbonate as a surrogate at this stage because the hyperchloreaemic acidosis associated with large volumes of 0.9% sodium chloride will lower bicarbonate levels)

**9.1.3.6. Other key strategies**

- **Identify and treat precipitating factors**
  - Infections, other stresses include pancreatitis, myocardial infarction, stroke, trauma, and alcohol and drug abuse
- **Prophylaxis for DVT**

**9.1.3.7. Conversion to subcutaneous insulin**

Intravenous Insulin infusion should be converted to an appropriate subcutaneous regimen when DKA is resolved and the patient is ready and able to eat.

Intravenous insulin infusion should not be discontinued for at least 30 to 60 minutes after the administration of the subcutaneous dose is given with a meal.
- **Restarting subcutaneous insulin for patients already established on insulin**

  The patient’s previous regimen should generally be re-started if their most recent HbA1c suggests acceptable level of control i.e. HbA1c <8.0%

- **Calculating the subcutaneous insulin dose in insulin-naïve patients**

  Estimate Total Daily Dose (TDD) of insulin = patient’s weight x 0.5 or 0.75. (Use 0.75 units/kg for those thought to be more insulin resistant i.e. teens, obese) Calculate Basal Bolus (QDS) Regimen or twice daily (BD) regimen

### 9.2. Hyperosmolar hyperglycemic state (HHS)

Hyperosmolar hyperglycemic state is a life threatening metabolic derangement that occur mostly in patients with type 2 DM who have some concomitant illness that leads to reduced fluid intake. Infection is the most common preceding illness and it is usually present in older patients with type 2 DM. HHS carries a higher mortality than DKA

#### 9.2.1. Diagnosis

- Hypovolaemia
- Marked hyperglycaemia (30 mmol/L or more) without significant ketonaemia (<3 mmol/L) or acidosis (pH>7.3, bicarbonate >15 mmol/L)
- Osmolality > 320 mOsm/kg

Alteration in mental status is common if osmolality> 330 mOsm/kg

#### 9.2.2. Management

##### 9.2.2.1. Fluid replacement

Fluid losses in HHS are estimated to be between 100 -220 ml/kg (6 -13 liters in a 60 kg person) with Na⁺ loss (300 -780 mmol), K⁺ loss (240 -360 mmol/L) and Cl⁻ loss (300 -900mmol)

The aim of treatment should be to replace approximately 50% of estimated fluid loss within the first 12 hours and the remainder in the following 12 hours

Use 0.9% sodium chloride solution to restore circulating volume and reverse dehydration.

Fluid replacement alone will lower blood glucose, serum sodium and osmolality

Rapid changes must be avoided – a safe rate of fall of plasma glucose of between 4 and 6 mmol/h is recommended
Other key strategies:

- **Identify and treat precipitating factors**
  Infections are the most common precipitating factor

- **Prophylaxis for DVT**
  As most patients are ill, dehydrated and bed bound, they are at increased risk of DVT

**Other Electrolyte Imbalances**

- Hypophosphatemia persisting beyond the acute phase of treatment of HHS, consider oral or IV replacement
- Magnesium replacement be considered if the patient is symptomatic
9.2.2.4. Recovery phase

Complete correction of electrolyte and osmolality abnormalities is unlikely to be achieved within 24 hours and too rapid correction may be harmful.

Early mobilization is recommended.

Intravenous insulin infusion can usually be discontinued and subcutaneous insulin can be started once patient is able to eat and drink but IV fluids may be required for longer if intake is inadequate.

For patients with previously undiagnosed diabetes or well controlled patients on oral agents, switching from insulin to the appropriate oral hypoglycaemic agent should be considered after a period of stability (weeks or months).
7.2. Management of Hypoglycaemia (3)

Management of hypoglycaemia in the hospital setting

Hypoglycaemia is defined as blood glucose < 72 mg/dL (4 mmol/L). Any patient with blood glucose < 72 mg/dL (4 mmol/L) with or without symptoms should be treated with 15 – 20 grams of quick acting carbohydrate as soon as hypoglycaemia is diagnosed.

The type of carbohydrate and the route of administration depend on the patient’s level of consciousness, ability to swallow and the need to keep the patient nil by mouth as described by the following algorithm.

![Algorithm for the management of hypoglycaemia](image)

- **Patient conscious, able to swallow and no need to keep the patient nil by mouth**
  - 25% dextrose 75 ml **orally**
  - Check CBG in 10-15 minutes
    - If CBG < 72 mg/dL repeat oral glucose up to 3 cycles
    - CBG < 72 mg/dL after 3 cycles
  - Repeat treatment until CBG > 72 mg/dL

- **Patient unconscious, uncooperative, unable to swallow or need to keep nil by mouth**
  - 25% dextrose 75 ml IV
    - 10% dextrose 150-200 ml IV over 15 minutes
  - Need to keep patient nil by mouth
    - **No**
      - Give a long acting carbohydrate orally e.g. 200-300ml glass of milk, normal meal
      - Do not omit patients next regular insulin or oral hypoglycaemic dose although dose review may be needed
    - **Yes**
      - 10% dextrose IV 100ml/h
      - If the patient was in insulin infusion, restart after review
Patients who experience hypoglycaemic symptoms but have a blood glucose level >72 mg/dL should be treated with a small carbohydrate snack only.

The following key points are important in management of hypoglycaemia

- Use oral glucose when possible to avoid complications of IV glucose administration and to maintain a smoother glycaemic control.
- **Avoid using 50% dextrose.** It is highly irritant and can cause serious complications. (severe thrombophlebitis and subsequent infection)
- Use a large bore cannula in a large vein when using IV dextrose
- If IV access is not available glucagon im can be given, if available.
- Do not omit next insulin or oral hypoglycaemic dose, but review the dose

**Further Assessment:**

- **Look for a cause for hypoglycaemia and correct it**
  - Erratic behavior – Incorrect dose/ technique, alcohol, vigorous exercises, skipping meals
  - Complication of diabetes –Renal impairment, autonomic neuropathy & hypoglycaemia unawareness
  - Other – Adrenal insufficiency

- **In the presence of hypoglycaemia unawareness or episode of severe hypoglycaemia:**
  - Re-evaluate treatment regimen
  - Insulin-treated patients: raise glycemic targets for several weeks to partially reverse hypoglycaemia unawareness and reduce recurrence
10. MANAGEMENT OF DIABETES IN SPECIAL SITUATIONS (5-7, 27-34)

10.1. Management of Diabetes in Chronic Kidney Disease

10.1.1. Measurement of Glycaemic Control

- HbA1c is affected by the severity of kidney dysfunction and the haematological complications of kidney disease.

- HbA1c is:
  - falsely decreased in haemolysis.
  - falsely elevated in acidosis and carbamylation of Hb.

- The “gold standard” is plasma glucose (FPG, PPG)
- Treatment decisions can be made by using daily glucose monitoring.

10.1.2. Pharmacological Treatment

- Clearance of many drugs and insulin is decreased by kidney disease leading to frequent hypoglycaemic episodes.
- The greatest risk is in patients with moderate to severe CKD (Stages 3–5).

**Insulin**

- All the available insulin preparations can be used in CKD.
- Insulin types and doses must be individualized to each patient and their level of CKD.

**Oral agents**

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
<th>CKD Stage 3–5</th>
<th>Dialysis</th>
<th>Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biguanides</td>
<td>Metformin</td>
<td>eGFF 30-45mL/min/1.73 m2 max. dose 1,000mg/day</td>
<td>Avoid</td>
<td>Lactic acidosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>eGFR &lt;30 mL/min/1.73 m2 – discontinue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulphonylurees</td>
<td>Tolbutamide</td>
<td>Use with caution</td>
<td>Avoid</td>
<td>Hypoglycaemia</td>
</tr>
<tr>
<td></td>
<td>Glibenclamide</td>
<td>Avoid</td>
<td>Avoid</td>
<td>Hypoglycaemia</td>
</tr>
<tr>
<td>Drug</td>
<td>Glipizide</td>
<td>Gliclazide</td>
<td>Glimepiride</td>
<td>α-Glucosidase inhibitors</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-----------</td>
<td>------------</td>
<td>-------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td></td>
<td>No dose adjustment</td>
<td>No dose adjustment</td>
<td>Low dose: 1 mg/day</td>
<td>Acarbose</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Avoid Hypoglycaemia</td>
</tr>
</tbody>
</table>

**10.2. Management of Diabetes in patients with heart failure**

- Since 2008 FDA has recommended to conduct cardiovascular safety trials for all new anti-diabetic drugs.

- Selection of anti-diabetic medications has to be done cautiously in patients with heart failure, due to the risk of fluid retention caused by certain drugs and the risk of lactic acidosis in decompensate state.

- Dose adjustment or complete withdrawal of some drugs is necessary in parallel to the severity of cardiac failure (Table 17).
<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
<th>NYHA 1-2</th>
<th>NYHA 3-4</th>
<th>Complications/ Special remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Biguanides</strong></td>
<td>Metformin</td>
<td>can be used provided eGFR&gt;30ml /min/1.73m²</td>
<td>Avoid</td>
<td>Discontinue during episodes of acute heart failure due to the risk of lactic acidosis</td>
</tr>
<tr>
<td></td>
<td>Glibenclamide/glimepiride</td>
<td>Limited data Available, use with caution</td>
<td>Limited data Available, use with caution</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gliclazide / Glipizide/Tolbutamide</td>
<td>No dose adjustment</td>
<td>use with caution</td>
<td></td>
</tr>
<tr>
<td><strong>Sulphonylurea</strong></td>
<td>Pioglitazone</td>
<td>Better avoided</td>
<td>Contraindicated</td>
<td>Worsen heart failure by fluid retention and increased hospitalization.</td>
</tr>
<tr>
<td><strong>α-glucosidase inhibitors</strong></td>
<td>Acarbose</td>
<td>Safe. But can lead to malabsorption of cardiac drugs</td>
<td>Safe. But can lead to malabsorption of cardiac drugs</td>
<td>Interact with drug absorption</td>
</tr>
<tr>
<td><strong>Meglitinides</strong></td>
<td>Repaglinide</td>
<td>No safety data available. Better avoided</td>
<td>No safety data available. Better avoided</td>
<td></td>
</tr>
<tr>
<td><strong>DPP 4 inhibitors</strong></td>
<td>Sitagliptin</td>
<td>No dose adjustment</td>
<td>No dose adjustment</td>
<td>No added risk of worsening of heart failure</td>
</tr>
<tr>
<td><strong>Saxagliptin</strong></td>
<td>Use with caution</td>
<td>Use with caution</td>
<td>Increasing hospitalization due to heart failure reported.</td>
<td></td>
</tr>
<tr>
<td><strong>Meglitinides</strong></td>
<td>Alogliptin</td>
<td>Safe to use</td>
<td>Safe to use</td>
<td></td>
</tr>
<tr>
<td><strong>GLP-1</strong></td>
<td>Exenatide</td>
<td>Safe to use</td>
<td>Safe to use</td>
<td></td>
</tr>
<tr>
<td><strong>SGLT 2 inhibitors</strong></td>
<td>Empagliflozin</td>
<td>Safe to use</td>
<td>Safe to use</td>
<td></td>
</tr>
<tr>
<td><strong>Insulin</strong></td>
<td>Use with caution</td>
<td>Use with caution</td>
<td>Use with caution</td>
<td></td>
</tr>
</tbody>
</table>
10.3. Management of diabetes in patients with liver dysfunction

- The liver is a primary site of drug metabolism and the impairment of drug metabolism is proportional to the liver dysfunction.
- Risk of hypoglycaemia and lactic acidosis is increased in severe liver dysfunction
- Therefore selection of antidiabetic drugs and their dose adjustments should be done according to the severity of liver disease (Table 18).

<table>
<thead>
<tr>
<th>Table 18: Hypoglycaemic agents in Liver dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Class</strong></td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>Biguanides</td>
</tr>
<tr>
<td>Sulphonylurea</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Thiazolidinedione</td>
</tr>
<tr>
<td>α-glucosidase inhibitors</td>
</tr>
<tr>
<td>Meglitinides</td>
</tr>
<tr>
<td>DPP 4 inhibitors</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>GLP-1</td>
</tr>
<tr>
<td>SGLT 2 inhibitors</td>
</tr>
<tr>
<td>Insulin</td>
</tr>
</tbody>
</table>
10.4. Peri-operative Care in a Diabetic Patient

- Elective surgery should be postponed whenever possible if glycaemic control is poor (HbA1c ≥ 9%).
- Blood glucose should be kept between 80-180 mg/dl during the peri-operative period
- Preoperative risk assessment should be done for patients at high risk for ischemic heart disease and those with autonomic neuropathy or renal failure.
- Patients who undergo minor surgery which require fasting should omit their morning oral hypoglycemic medication.
- Patients on Insulin should be on long acting basal insulin given in the morning.
- Patients undergoing major surgery may require insulin – glucose infusion during surgery as well as during post operative period until oral intake is resumed.
- Once patient has resumed oral feeding blood glucose can be controlled by basal long acting insulin plus short acting insulin at meal times.

10.6. Management of Diabetes in acute illness

- All patients admitted to hospital should have their blood glucose tested.
- Hyperglycaemia in the hospital may be due to previously known diabetes, previously undiagnosed diabetes, or stress-related hyperglycaemia.
- Blood glucose levels persistently higher than 140 mg/dL (7.8 mmol/ L) should be considered for treatment in hospitalized patients.
- HbA1C values > 6.5% suggests undiagnosed diabetes that preceded hospitalization.

Non-critically ill patients

- Individualized care under a specialist is recommended.
- Basal insulin or a basal plus bolus correction insulin regimen is preferred.
  - Total daily dose of insulin:
    - 0.5–0.7 units/kg for Type 1 DM
    - 0.4–1.0 units/kg or more for patients having Type 2 DM
- Use 50% of the calculated daily dose as basal insulin (divided in two doses if Isophane insulin is used) and rest as premeal bolus in divided doses.
- If the premeal glucose is high extra dose of bolus insulin can be given (Correction-dose of insulin).
- Traditional sliding scale insulin regimens are no longer recommended and when used as sole therapy, result in large swings in blood glucose levels.

- Continuation of home regimens including oral antihyperglycemic medications may be appropriate in selected stable patients taking normal meals at regular meals under specialist advice.

**Blood Glucose Targets**

<table>
<thead>
<tr>
<th>Premeal</th>
<th>&lt;140 mg/dL (7.8 mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBG</td>
<td>&lt; 180 mg/dL (10 mmol/L)</td>
</tr>
</tbody>
</table>

- Hypoglycaemia should be avoided and treatment regimen should be modified when blood glucose values are <70 mg/dL (3.9 mmol/L).

**Critically ill patients**

- In critically ill ICU patients, insulin infusion should be started if blood glucose levels is >180 mg/dL.
- Blood glucose levels should be maintained between 140 and 180 mg/dL (7.8–10.0 mmol/L) while the lower limit is preferred.
- In selected patients lower blood glucose target (<140 mg/dL) may be appropriate. However targets less than 110 mg/dL (6.1 mmol/L) are not recommended.
- Transition from IV insulin infusion to subcutaneous insulin:
  - Calculate total daily dose used in infusion (Calculate the total insulin dose given for the last 6 hours and multiply it by four to get the daily requirement) and give it as basal bolus regimen
  - Continue infusion for another 1–2 h after the first subcutaneous dose.
<table>
<thead>
<tr>
<th>Blood glucose (mg/dL)</th>
<th>Insulin infusion(units/hour)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A1</td>
</tr>
<tr>
<td>&lt;100</td>
<td>0</td>
</tr>
<tr>
<td>100-109</td>
<td>0</td>
</tr>
<tr>
<td>110-119</td>
<td>0.5</td>
</tr>
<tr>
<td>120-149</td>
<td>1</td>
</tr>
<tr>
<td>150-179</td>
<td>1.5</td>
</tr>
<tr>
<td>180-209</td>
<td>2</td>
</tr>
<tr>
<td>210-239</td>
<td>2</td>
</tr>
<tr>
<td>240-269</td>
<td>3</td>
</tr>
<tr>
<td>270-299</td>
<td>3</td>
</tr>
<tr>
<td>300 - 329</td>
<td>4</td>
</tr>
<tr>
<td>330-359</td>
<td>4</td>
</tr>
<tr>
<td>&gt;360</td>
<td>6</td>
</tr>
</tbody>
</table>

- Glycaemic target- 140-180mg/dL (Not less than 110mg/dL)
- Standard infusion: 100 units of insulin/100 mL 0.9% NaCl via infusion device (1units/1mL)
- Enough glucose must be provided to avoid starvation ketosis and prevent hypoglycaemia: At least 5-10g of glucose/hour (D5W: 5% Dextrose in water or D5W.NS: 5% Dextrose in normal saline at 100–200mL/hour or equivalent,TPN, enteral feeding, etc.)
- Starting the Infusion: Once BG> 120 mg/dl
  - Algorithm 1: Start here for most patients.
  - Algorithm 2: start here if receiving glucocorticoids, previously on high total daily dose of insulin etc.
- Moving from Algorithm to Algorithm:
  - Moving Up: if the blood glucose is above the goal range & does not change by at least 60mg/dL within 1 hour.
  - Moving Down: When glucose is <110 mg/dL for 2hrs or decreases >60 mg/dl in 1 hour
- Patient Monitoring:Do hourly capillary glucose until glucose is within goal and may extend to 2-4 hourly if stable.
- Treatment of hypoglycaemia (blood glucose<70mg/dL)
Stop insulin infusion drip and give IV 50% Dextrose (Awake-25ml, Not awake-50ml)

- Recheck blood glucose every 20min and repeat 25mL of 50% dextrose
- Restart insulin infusion once blood glucose is >110mg/dL for 2 checks
- Restart drip with lower algorithm

This algorithm is not intended to be used for those individuals with Type 1 DM, diabetic ketoacidosis or hyperglycaemic hyperosmolar states.

10.5. Diabetes in Pregnancy (5,6)

Tight glycaemic control in the first trimester is crucial to prevent fetal congenital malformations. Therefore preconception planning is of vital importance.

All Sri Lankan pregnant women should initially undergo screening for preexisting diabetes at Anti Natal Clinic booking visit by HBA1c or fasting blood glucose.

10.5.1. Diagnosis of Diabetes in Pregnancy

All pregnant women who attend the booking visit should be screened for diabetes in pregnancy with 2hr 75 g OGTT. If the screening test becomes negative, those women should be retested at a POA of 24 -28 weeks.

IADPSG recommended diagnostic criteria (2hr 75 g OGTT) for diagnosis

Fasting plasma glucose: \( \geq 92 \text{ mg/dL} \) (5.1 mmol/L)
One hour plasma glucose \( \geq 180 \text{ mg/dL} \) (10 mmol/L)
2 hr plasma glucose: \( \geq 153 \text{ mg/dL} \) (8.5 mmol/L)

10.5.2. Pre-pregnancy counselling and workup in Pre existing Diabetes

- Achieve the best possible glycaemic control before conception.
- Target HbA1c is <6.5%.
- Women with an elevated HbA1c value above 8.0% should be discouraged from becoming pregnant until their control can be improved and appropriate contraceptive advice should be provided.
- Initiate insulin to get ideal control
- Use of metformin should be under specialist care.
- Assess established diabetes complications before conception.
o Detailed renal and retinal assessment

- Stop ACE inhibitors, ARBs, Statins, fibrates and niacin before conception or as soon as pregnancy is confirmed.
- Alternative antihypertensive agents suitable for use during pregnancy (Nifedepine, Methyl Dopae, Prazosin, Hydralazine and Labetalol) should be substituted.
- Women with diabetes with unplanned or unexpected pregnancy, should be referred to a specialist immediately

10.5.3. Management of Diabetes during Pregnancy

- Encourage self-monitoring of blood glucose levels - both fasting and postprandial, preferably 2 h after a meal.

<table>
<thead>
<tr>
<th>Timing</th>
<th>Target in mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premeal</td>
<td>≤95 mg/dl</td>
</tr>
<tr>
<td>1 h after a meal</td>
<td>≤140 mg/dl</td>
</tr>
<tr>
<td>2 h after a meal</td>
<td>≤120 mg/dl</td>
</tr>
</tbody>
</table>

- Women with insulin-treated diabetes should test blood glucose levels at bed time as well.

1. **Lifestyle management**

**Medical Nutrition Therapy**

- Advice should be individualized and should be administered by a nutritionist/dietician.
- Calorie requirement in pregnancy is 30 Kcal/kg/day and in overweight pregnant ladies, it is 25 kcal/kg/day or less.
- Women with pre-existing diabetes who had previous nutritional advice need to be revised and reviewed during pregnancy.
- Dietary advices should be reemphasized at each clinic visit.

**Exercise**

- A minimum of 30 minutes exercise on most days of the week is recommended during a normal pregnancy (e.g. walking, swimming, cycling and aerobics).

2. **Insulin use during pregnancy**
• Lifestyle measures may be adequate in some, while others may need insulin from the beginning.
• Pre-mixed or basal bolus regimens are the most suitable.
• Women on insulin should be advised of the risks of hypoglycaemia particularly in the first trimester.

3. **Oral glucose-lowering agents in pregnancy**

• Metformin can be used with caution under specialist care in pregnancy and breastfeeding
• All other oral hypoglycaemic agents should be discontinued before pregnancy and substituted with insulin.

4. **After delivery**

• Women with preexisting diabetes before conception:
  - Require lower doses of insulin post partum.
  - Should be counseled on contraception and pre-conception care.

• Women with gestational diabetes:
  - At discharge, reinforce lifestyle modification.
  - Screen for persistent diabetes at 6–12 weeks postpartum, using OGTT
  - Re screen annually
  - Those who have pre diabetes should receive lifestyle interventions or metformin to prevent diabetes.
Annexure 1: Sample meal plans for patients with diabetes

<table>
<thead>
<tr>
<th>Meal plan-1 (1800 kcal)</th>
<th>Meal plan-2 (1300 kcal)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>For weight maintenance in most</strong></td>
<td><strong>For weight loss in most</strong></td>
</tr>
<tr>
<td><strong>Breakfast</strong></td>
<td><strong>Breakfast</strong></td>
</tr>
<tr>
<td>Non-fat milk 1 cup (morning tea)</td>
<td>Non-fat milk 1 cup (morning tea)</td>
</tr>
<tr>
<td>Rice 2 cups</td>
<td>Rice 1 cup</td>
</tr>
<tr>
<td>Non-starchy vegetables 3 cups</td>
<td>Non-starchy vegetables 3 cups*</td>
</tr>
<tr>
<td>Fish / Meat 1-2 pieces</td>
<td>Fish / Meat 1 piece</td>
</tr>
<tr>
<td>Or</td>
<td>Or</td>
</tr>
<tr>
<td>Green gram / Chick peas 2 cups with “Lunumiris”</td>
<td>Green gram / Chick peas 1 cup with “Lunumiris”</td>
</tr>
<tr>
<td><strong>Morning snack</strong></td>
<td><strong>Morning snack</strong></td>
</tr>
<tr>
<td>Fruits 1 cup (e.g. 1 small banana)</td>
<td>Fruits 1 cup (e.g. 1 small banana)</td>
</tr>
<tr>
<td><strong>Lunch</strong></td>
<td><strong>Lunch</strong></td>
</tr>
<tr>
<td>Rice 2 cups</td>
<td>Rice 1 cup</td>
</tr>
<tr>
<td>Non-starchy vegetables 3 cups</td>
<td>Non-starchy vegetables 3 cups*</td>
</tr>
<tr>
<td>Fish / Meat 1-2 pieces</td>
<td>Fish / Meat 1 piece</td>
</tr>
<tr>
<td><strong>Afternoon snack</strong></td>
<td><strong>Afternoon snack</strong></td>
</tr>
<tr>
<td>Non-fat milk 1 cup</td>
<td>Non-fat milk 1 cup</td>
</tr>
<tr>
<td>Fruits 1 cup or 2 sugar-free biscuits</td>
<td>Fruits 1 cup or 2 sugar-free biscuits</td>
</tr>
<tr>
<td><strong>Dinner</strong></td>
<td><strong>Dinner</strong></td>
</tr>
<tr>
<td>Red string hoppers – 5-7</td>
<td>Red string hoppers – 3-5</td>
</tr>
<tr>
<td>Non-starchy vegetables 2 cups</td>
<td>Non-starchy vegetables 2 cups*</td>
</tr>
<tr>
<td>Dhal ½ cup</td>
<td>Dhal ½ cup</td>
</tr>
<tr>
<td>Or</td>
<td>Or</td>
</tr>
<tr>
<td>Rice 2 cups</td>
<td>Rice 1 cup</td>
</tr>
<tr>
<td>Non-starchy vegetables 2 cups</td>
<td>Non-starchy vegetables 2 cups*</td>
</tr>
<tr>
<td>Fish / Meat 1-2 pieces</td>
<td>Fish / Meat 1 piece</td>
</tr>
<tr>
<td><strong>Late night snack</strong></td>
<td><strong>Late night snack</strong></td>
</tr>
<tr>
<td>Non-fat milk 2 cups or 2 sugar-free biscuits or fruits 1 cup</td>
<td>Non-fat milk 1 cup or 2 sugar-free biscuits</td>
</tr>
</tbody>
</table>

* Vegetables should be cooked without coconut milk
be cooked without coconut milk
### Annexure 2: Different Insulin types

<table>
<thead>
<tr>
<th>Insulin type</th>
<th>Onset of action</th>
<th>Peak action</th>
<th>Duration of action</th>
<th>Colour</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ultra short acting/ Rapid acting insulin analogue:</strong> insulin lispro, insulin aspart, insulin glulisine</td>
<td>&lt;15 min</td>
<td>1-2 hrs</td>
<td>4-6 hrs</td>
<td>Clear</td>
</tr>
<tr>
<td>Usually taken before or with a meal to cover the post prandial blood sugar elevation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Short acting Insulin:</strong> Regular Human Insulin</td>
<td>½-1 hr</td>
<td>2-4hrs</td>
<td>6-8hrs</td>
<td>Clear</td>
</tr>
<tr>
<td>Taken 30 min before meal to cover the post prandial blood sugar elevation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Intermediate acting:</strong> NPH</td>
<td>1-2 hr</td>
<td>6-10 hrs</td>
<td>&gt;12 hrs</td>
<td>Cloudy</td>
</tr>
<tr>
<td>Often combined with rapid or short acting insulin (Pre-Mixed insulin) and taken twice a day</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Can be used as a basal insulin at initiation of insulin therapy (Single bedtime dose)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Long Acting:</strong></td>
<td>3-4 hrs</td>
<td>No defined peak</td>
<td>12-&gt;24hrs</td>
<td>Clear</td>
</tr>
<tr>
<td>Insulin Glargin, Insulin Detemir, Insulin Degludec</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Usually used as a basal insulin and given once or twice daily</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Can be combined with short/ rapid acting insulin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
References


12. Rydén L, Grant PJ, Anker SD, BerneC, Cosentino F et al. ESC Guidelines on diabetes, prediabetes & cardiovascular diseases developed in collaboration with the EASD: the Task Force on diabetes, pre-


12. Edward W. Gregg, Silvio E. Inzucchi, Mark E. Molitch, John M.Morton, Robert E. Standards of Medical Care in Diabetes—2015. Diabetes Care 2015;38(Suppl. 1)


